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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,703	07/09/2003	Stephen J. Benkovic	00-387-P	5892

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/615,703	BENKOVIC ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,12-14,16,41 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,12-14,16,41 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/2007 has been entered.

Withdrawn Rejection

In view of the amendments to the claims and applicants' arguments the 35 USC 102 rejections over Brasseur et al, Heithoff et al and Mahan et al have been withdrawn.

Claims Status

Claims 1-3, 5, 12-14, 16, 41 and 44 are pending and under consideration.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, as amended, are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed method for treating an animal against a bacterium induced disease comprising the step of inhibiting DNA methyltransferase activity in said bacterium e.g., Brucella species would read on the natural method or processes (e.g., immune response method or reaction) in an animal of inhibiting i.e., producing antibody against the bacterium(foreign or antigen) inducing disease such as the bacteria Brucella.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5, 12-14, 16, 41 and 44, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

the application was filed, had possession of the claimed invention.

The specification does not provide an adequate written description of a methyltransferase inhibitor that has been administered to a mammal to therapeutically treat mammals afflicted with a bacterium induced disease such as Brucella species. The original specification describes a method of defining the genes of the bacterium responsible for methyl transferase. Furthermore, the specification discloses the different processes by which an inhibitor can be obtained. However, none describes an inhibitor that has treated a bacterium induced disease specifically in human patients. The disclosure as of the filing date does not describe e.g., the kind or type of inhibitor that has been employed in the method to treat mammals.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 12-14, 16, 41 and 44, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the step by which inhibiting DNA methyltransferase activity is achieved. The method does not recite any step/element by which DNA methyltransferase activity has been inhibited.

2. Claim 3 is indefinite and repetitive since DNA methyltransferase inhibited is an enzyme inhibition, especially since the specification does not describe any other enzyme inhibition except methyltransferase. This rejection has similar import to claim 14.

3. Claim 5 is indefinite since an animal is not a human patient.

4. Claim 12 is indefinite as to what would be considered a therapeutically effective dose of a methyltransferase inhibitor administered to a mammal. The specification does not disclose or identify a single inhibitor. Thus, it is unclear as to the basis of the dosage considered to be therapeutically effective. This rejection has similar import to claim 41.

5. Non-sequitur for "said DNA" in claims 13 and 14 and "said animal" in claim 16. The base claim 12 recites only methyltransferase and a mammal, respectively.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5, 12-14, 16, 41 and 44, as amended, are rejected on the ground of nonstatutory double patenting over claims 1-5 of U. S. Patent No. 6413751('751 patent) since the

claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: the instant claimed treatment method that inhibits the disease induced by e.g., Brucella is obvious over the isolated DNA methyltransferase of the '751 patent. The isolated gene compound DNA methyltransferase is obviously the compound inhibited by the treatment method. See e.g., col. 4, lines 5-20. Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5, 12-14, 16, 41 and 44, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Vermeulen et al (5872104) in view of Barney et al (6068973)and Lonetto et al (6165762).

Vermeulen discloses throughout the patent at e.g., col. 3, lines 4-64:

> A method comprising administering to an animal (including a human patient) that has, or is suspected to have a microbial or bacterial infection, a therapeutically effective amount of pharmacologically acceptable antimicrobial agent formulation in combination with a therapeutic amount of a pharmacologically acceptable formulation of a second agent effective to inhibit methylation, e.g., effective to inhibit RNA methylation. The invention may thus be employed to treat both systemic and localized microbial and bacterial infections by introducing the combination of agents into the general circulation or by applying the combination, e.g., topically to a specific site, such as a wound or burn, or to the eye, ear or other site of infection.
>
> The "second agents" for use in the invention are generally methylation inhibitors, and are also referred to herein as "inhibitors" and "modifiers". The second agent inhibitors should be used in amounts effective to inhibit methylation in a microorganism or bacterium, as exemplified by an amount effective to inhibit RNA methylation, synthesis and/or maturation in an MLS-susceptible bacterium. Suitable amounts effective to inhibit methylation will be known, or readily identifiable, to those of skill in the art. Effective inhibitory amounts are the amounts that have previously been shown in the scientific literature to inhibit methylation generally or to inhibit a specific methylation step. In addition to the present disclosure and the references specifically incorporated herein, there is considerable scientific literature concerning methylation inhibitors that may be utilized in light of the inventors'

discovery that such compounds may be effectively combined with antibiotics and other antimicrobial agents.

Amounts effective to inhibit methylation may also be measured, rather than identified from the published literature. Most simply, this is achieved by determining the amount effective to increase microbial or bacterial killing when used in combination with an antimicrobial agent, i.e., by determining an amount effective to reduce antimicrobial resistance. The determinations of effective inhibitory amounts and therapeutic doses will be routine to those of skill in the art given the teachings of the present disclosure, including the detailed methodology and the effective amounts of various agents disclosed, e.g., in Table 8 and throughout the detailed examples. Importantly, the inhibitors shown in Table 8 are generally representative of the different groups of inhibitors identified by the inventors, i.e., compounds capable of inhibiting RNA methyltransferases; SAH hydrolase; SAM synthetase (via inhibiting glutathione synthetase); dihydrofolate reductase (DHFR); and also, agents that inhibit polyamine synthesis.

Vermuelen further discloses at e.g., col. 77, lines 27-35:

Guinea pigs infected by Brucella canis and treated with liposome-entrapped streptomycin were found to be free of bacteria, whereas animals treated with the free drug, for the same schedule of administration, showed only a minor reduction in the number of surviving bacteria (Fountain et al., 1985).

While Vermuelen discloses in general bacteria however the other species such as Agrobacterium, Rhizobium and Helicobacter species are not disclosed by Vermuelen. However, Barney et al throughout the patent discloses the different bacterial species such as Agrobacterium, Rhizobium and

Helicobacter. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to treat other bacteria in the method of Vermeulen. Vermeulen teaches treatment of bacteria in general and does not seem to limit to those disclosed therein. It would be within the ordinary skill in the art at the time the invention was made to choose the specific bacteria depending upon the bacteria desired to be treated. The bacteria Agrobacterium, Rhizobium and Helicobacter are known to have been treated in the art whether via the mechanism of DNA methyltransferase inhibition or by other mechanistic pathway as evidenced by Lonetto et al, which discloses at e.g., col. 19, lines 50-67:

> Helicobacter pylori (herein H. pylori) bacteria infect the stomachs of over one-third of the world's population causing stomach cancer, ulcers, and gastritis (International Agency for Research on Cancer (1994) Schistosomes, Liver Flukes and Helicobacter Pylori (International Agency for Research on Cancer, Lyon, France; http://www.uicc.ch/ecp/ecp2904.htm). Moreover, the international Agency for Research on Cancer recently recognized a cause-and-effect relationship between H. pylori and gastric adenocarcinoma, classifying the bacterium as a Group I (definite) carcinogen. Preferred antimicrobial compounds of the invention (agonists and antagonists of apt) found using screens provided by the invention, particularly broad- spectrum antibiotics, should be useful in the treatment of H. pylori infection. Such treatment should decrease the advent of H. pylori-induced cancers, such as gastrointestinal carcinoma. Such treatment should also cure gastric ulcers and gastritis.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
January 7, 2006